pentine and isoniazid, once weekly for 3 months, provides highly effective chemoprophylaxis.

Other agents: Information about *in vitro* and to a lesser extent *in vivo* activities of two oxazolidinone compounds (U-100592 and U-100766) and a nitroimidazole compound (PA-824) suggest a possible future role for one or more of these agents.

In conclusion, development of effective new antimycobacterial agents has lagged far behind the need for them. Improved public–private sector collaboration is needed to remedy the deficiency.

Clinical implications of antibiotics resistance in developing countries

S126 Use and misuse of antibiotic policies to control drug resistance

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The use of antibiotics has led to the emergence of a variety of resistant bacteria which have clearly added to the challenge of controlling infections with new agents.

Misuse of antibiotics is responsible for a general pool of resistant strains in the population where there is unrestricted sale of antibiotics, i.e. over the counter.

Appropriate use of antibiotic policies to control drug resistance should be encouraged and implemented. In order to do so, an antibiotic committee should be responsible for the formulation and supervision of an antibiotic policy.The policy will improve patient care by considered use of antibiotics for prophylaxis and therapy, make better use of finance, retard the emergence of multiple antibiotic-resistant bacteria and improve education of junior doctors by providing guidelines for appropriate therapy.

The antibiotic committee will have to make rational choices among equivalent antibiotics and classes of drugs in order to select the least expensive, most effective agents.Cost should determine the selection when microbiological, pharmacologic and other relevant properties are similar.

Data on antibiotic susceptibility of bacterial isolates from the local area will assist the committee in producing effective guidance for the patient population.The laboratory should give data on the extent of resistance to a particular antibiotic. When no local microbiology laboratory exists, the antibiotic policy should be based upon a basic formulary; when resources for microbiology are scarce, priority should be given to examination of samples from nosocomial life-threatening cases.

Inappropriate use of antibiotic policies has limited the choice of antibiotics, and there is a need for more prudent use of antibiotics in the treatment of infections, especially in developing countries.

S127 The clinical relevance of antibiotic resistance for the management of pneumonia in developing countries

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There is now widespread in vitro resistance to the common drugs used for the management of pneumonia in developing countries. Data from both developed and developing countries, however, show that more than 99% of pneumococci identified as penicillin resistant in the laboratory can be treated by adequate intravenous doses of penicillin or ampicillin. Trimethoprim–sulfamethoxazole is less active than amoxycillin for the management of severe pneumonia in developing countries, The lesser activity of trimethoprim–sulfamethoxazole was not directly related to levels of antimicrobial resistance to that agent, suggesting that amoxycillin is intrinsically more active against the common bacterial agents causing pneumonia. Macrolide resistance has emerged as a major problem in Asia, with 80% of pneumococci isolated from children in China exhibiting resistance to this class of agent. Guidelines for the management of pneumonia recommend that the breakpoints for penicillin resistance should be increased, so that clinicians are not faced with dilemma of treating 'resistant' strains with penicillin. Nasopharyngeal screening programs give data on antimicrobial resistance that are comparable to those obtained from sterile-site specimens. More data are required on the impact of penicillin resistance on the oral management of pneumonia. Current data would suggest that, where affordable, oral amoxycillin should replace trimethoprim–sulfamethoxazole as the drug of choice for the management of moderate to severe pneumococcal pneumonia in developing countries.

Short course antibiotic therapy with macrolides

S128 Risk–benefit of short-course therapy with macrolides

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Due to favorable pharmacokinetics, shorter therapeutic regimens are now used with some of the newer macrolides. These products are characterized by rapid and substantial intracellular accumulation, particularly in the lysosomes, followed by slow release from the cells, so that intracellular concentrations can surpass blood concentrations by several hundred-fold. Among macrolides, azithromycin displays the most important intracellular accumulation, making possible simplified dosing. Most macrolide-susceptible respiratory tract infections can be efficiently treated by once-a-day dosing for 3 days with azithromycin; genital and eye infections caused by *Chlamydia trachomatis* are controlled with a single dose of the drug. There is a trend to extend the concept of a single therapeutic dose in respiratory infections, more particularly in acute otitis media and pharyngitis, with the same total dose as in the more conventional treatment (30 mg/kg for a child). Compared to the 3-day regimen, the single dose assures the same serum half-life and AUC, but maximum antibiotic concentrations appear earlier (at day 1 versus day 3) and reach higher levels. In theory, this could provide improved efficacy and limit the risk of resistance selection. The single dose could lead to 100% compliance if the drug is taken in presence of heath personnel. Improved compliance decreases the risk of therapeutic failure and the cost. Possible inconvenience includes more side effects associated with drug concentrations, particularly the gastrointestinal manifestations.

S129 Overview of azithromycin therapy

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Azithromycin (AZ) has proven in vitro bacteriologic activity against many important community-acquired Gram-positive and Gram-negative pathogens, as well as the atypical respiratory pathogens. In

addition, its pharmacokinetics distinguish AZ from the traditional antibiotics. After the initial rapid absorption, AZ levels in tissues remain above the minimum inhibitory concentrations for these organisms for up to 8 days. The unique pharmacokinetics of AZ enable once-daily administration for only 3 days to provide effective therapy comparable to that achieved with other antimicrobial agents given as multiple daily doses for up to 10 days. A meta-analysis of randomized, comparative clinical studies comparing AZ with penicillins, cephalosporins and macrolides has demonstrated its comparable clinical and bacteriologic efficacy in the treatment of adults with community-acquired upper or lower respiratory tract infections. By the end of treatment, more than 90% of patients had a successful clinical response, and nearly 90% of the bacteria detected before treatment were eradicated from the respiratory tract. In clinical studies in more than 1500 adults receiving a once-daily, 3-day course of therapy, AZ was as well tolerated as comparator agents, with a similar incidence of laboratory abnormalities and discontinuations from treatment. When used to treat children, AZ has proved equally effective and safe. A combination of once-daily dosing, a shorter course of therapy compared with first-line agents, and good toleration of AZ, all contribute to patient compliance, and may help to optimize the treatment of community-acquired respiratory tract infections.

S130 Single-dose therapy in otitis media

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Acute otitis media (AOM) is one of the most common infectious diseases of childhood and also one of the most common conditions for antimicrobial prescription in pediatrics. Bacterial pathogens are isolated from middle-ear fluid in about two-thirds of patients and, in most parts of the world, antimicrobial therapy is considered standard therapy. The choice of antibiotic is based on antimicrobial spectrum, pharmacokinetic properties, safety and cost. Although 10 days is currently considered the standard duration of therapy, poor compliance and drug-related side effects strongly suggest the need for shorter regimens. Single-dose ceftriaxone (CFT) has been approved in a number of countries as a therapeutic option. Published studies suggest clinical and bacteriologic results similar to those of standard 10-day therapy against standard agents; however, its use is limited by the incidence of gastrointestinal side effects, need for parenteral administration and possibility of selection for resistance. Azithromycin (AZ) is an azalide antibiotic with good in vitro activity against middle-ear pathogens, high middle-ear penetration and a prolonged half-life. In patients with AOM, a 3-day regimen of AZ had a similar clinical and bacteriologic efficacy rate to 10-day regimens of standard agents. A single-blind clinical trial comparing single-dose, oral AZ, 3-day AZ and single-dose intramuscular CFT, in children with AOM, was completed in Costa Rica. Of a total of 180 clinically evaluable patients, clinical cure and bacteriologic eradication was observed in 97% of patients in the single-dose AZ group, 98% in the 3-day AZ group and 100% in the CFT group (P=NS). Adverse events were infrequent in all three groups. These data suggest that larger clinical trials with single dose-AZ in pediatric patients are warranted.

S131 Azithromycin in hyperendemic trachoma

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Trachoma is the world's leading cause of preventable blindness: 600 million people live in endemic areas, with 6 million blind. To prevent blindness, long courses of topical tetracycline are given to children or entire communities (mass treatment). Oral antibiotics are more effective, but the long courses required are impractical in developing countries. Azithromycin, with a dosing advantage, and good anti-chlamydial activity, offers an intriguing possibility for trachoma control. In a multicenter trial, we evaluated community-wide treatment in trachoma-endemic villages in Egypt, Tanzania and The Gambia. Oral azithromycin, given weekly three times to assure coverage, was compared with 6 weeks of daily topical tetracycline. Among those with active trachoma, ocular chlamydial infection, as determined by ligase chain reaction (LCR), was detected in 50%. This dropped dramatically post-treatment (up to 90%) at all sites. Infection rates seen after azithromycin in Egypt and Tanzania were lower than after tetracycline; these low rates persisted. In contrast, in The Gambia, there was no difference in LCR positivity between groups by the 2-month follow-up, possibly due to high rates of inward migration of untreated individuals. At all sites, the year-end infection rates were significantly lower than at baseline. In practice, the benefits of oral azithromycin will be even greater, as compliance with topical tetracycline will be much lower than under our research conditions. Fewer oral doses are more convenient, less irritating and better tolerated than multiple doses of eye ointment. It will certainly require treatment of larger areas, and possibly retreatment, but community-wide treatment with azithromycin may provide control of blinding trachoma.

S132 Single-dose therapy of sexually transmitted diseases

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Compliance is a major consideration in the management of STDs. The development of drugs, such as azithromycin (AZ), with enhanced intracellular penetration and a prolonged half-life, has increased the possibility of single-dose therapy. The ideal antibiotic for single-dose treatment must be orally active against common pathogens, free of significant side effects and economic. AZ is highly active in vitro against the intracellular and cell-associated pathogens *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Ureaplasma urealyticum*, as well as against *Haemophilus ducreyi*. In general, macrolides are not reliable for the single-dose therapy of lower genital tract gonorrhoea. However, a single 1-g oral dose of AZ is effective, provided that the organism is known not to be macrolide resistant. Uncomplicated non-gonococcal genital infection is conventionally treated with a 7-day oral course of either a tetracycline or erythromycin. Neither is ideal, owing to gastrointestinal side effects and problems with compliance. Several controlled clinical trials have demonstrated that a single 1-g oral dose of AZ is as efficacious as a week's course of doxycycline or erythromycin. *Chlamydia* is reliably eradicated in both men and women, and the clinical response rate is around 85% with either single-dose AZ therapy or conventional multidose therapy, in both chlamydial and non-specific infection. Chancroid is the commonest bacterial cause of genital ulcer disease worldwide. A single 1-g oral dose of AZ is equivalent to a week's course of erythromycin, or a single IM dose of ceftriaxone. Side effects of oral AZ are comparatively mild. Pharmacoeconomic studies indicate that savings in total episode care should offset the higher basic cost of AZ.